EARLY DIAGNOSIS OF TUBERCULOSIS AS A MEASURE OF CONTROL,

ESPECIALLY THE RELATION OF TUBERCULIN THERETO *

WILLIAM A. EVANS, M.D.
CHICAGO

The Department of Health of Chicago began the registration of consumptives July, 1907. A rule was passed requiring it. At the time the number of available beds for consumptives was 325. These were for late cases. In addition the Tuberculosis Institute was maintaining a sanitarium for early cases. The capacity of that institution shortly after July was increased to twenty-six beds.

There are two tent colonies near the city. One, that of Drs. Pettit and Butterfield, was then in existence; that of the Homeopathic Medical Society was founded last year. The general hospitals were taking a few cases, generally without plain, straightforward acknowledgment of the fact, and lacking the better control which goes with candor.

The experiences of these institutions was that consumption was not being diagnosed early enough for successful handling. Occasionally a diagnosis was made when an arrest could be accomplished in less than five months. Rarely one was determined when an arrest in two or three months was possible. The usual favorable case, according to the opinion of the diagnostician, required from one to three years of expensive maintenance without any earning power during the interim. Returned to work with his disease arrested, his outlook was a life of diminished capacity for productive work with a high probability of recurrence of his disease.

Viewed strictly from the economic standpoint, it is doubtful if anything is gained by curing these two to three year cases. I have in mind one institution which has been confronted with a great dilemma, due to two factors: (1) The physicians in attendance are not diagnosing the disease until it has reached such a stage that more than two years are required for arrests; (2) the patients who constitute the clientele are not financially able to withstand the needed expense.

This, as you see, leaves another problem untouched—the late and dangerously contagious consumptive. Our provision for these patients is much more adequate than that in any other direction, as it is most immediately vital.

As a means to reporting, we adopted disinfection of premises previously occupied by tuberculous patients and the use of tuberculin. All such premises are disinfected and instructions for cleaning are given. The number of premises disinfected for tuberculosis since Jan. 1, 1908, is 1,268, with 6,673,500 cubic feet. It has been unopposed, except in two minor instances. We have given away more than 500 doses of tuberculin. Our *Bulletin* has carried seven notices as to early diagnosis and the use of tuberculin therein; 928 cases of living tuberculosis have been reported since Jan. 1, 1908. The newly established tuberculosis dispensaries, six in number, are valuable factors in the discovery of consumption.

The methods employed are three days' preliminary observation of pulse and temperature, at 8 a. m., 12 noon, and 8 p. m. Late in the evening of the third day 4 milligrams of old tuberculin are given hypodermically. The temperature and pulse observations are made every two hours during the next day. A rise in temperature to 101.5 F. + is held to be a reaction, when there is a rise of pulse of 15 beats, a general and local reaction. As soon as the reaction is definite, control of the neuralgias with phenacetin is advised.

We have also made use of the ophthalmic tuberculin test. We reserve judgment as to its value. We are now engaged in testing 1,500 cows with it, doing controls with the hypodermic method. We endeavored to determine that dose which would give clear-cut, definite reactions in those cases which were of some clinical importance. A larger dose would discover some cases with quite well encapsulated small lesions, oftentimes limited to the lymphatic glands. Many of these cases are of small clinical importance and should not be handled as one would a clinical case. A smaller dose would give reactions so mild that a man of considerable experience would be required to interpret them.

I have in mind now a case of very chronic pleural infection in which the other method of administration gave a result which was variously interpreted by many observers.

The method which begins with a progressively increasing dose is open to the objection that greater skill is required in interpreting the result, and the coefficient of certainty is lowered and the progressing immunity adds a factor of uncertainty. While there is not the same degree of immunity as veterinarians have noted with regard to the use of full doses, it is, in some degree, a factor. I know of no observations tending to prove that the principle of sensitizing has any bearing on the conditions which obtain in examinations for diagnosis.

The objection is that the patient is uncomfortable for twenty-four hours. The claim that there is danger will be discussed separately. The discomfort can be made slight with antineuralgics. In my experience, the patients have recognized that the proceeding meant too much to be obfuscated by minor considerations.

The second question is the danger. I have no evidence that leads me to believe that in this respect the minor dose method differs from the other. Therefore, the question of danger is the danger of the use of tuberculin for diagnostic purposes. The arguments for its danger may be divided into two groups, (1) the histologic and bacteriologic, and (2) the clinical. The first teaching, that of Virchow, was that miliary generalization of tuberculosis was due to degeneration of the granuloma tissue with discharge into the blood vessels. The proof now is quite conclusive, to my mind, that blood generalization is by thoracic duct transmission. Longcope and Whipple have proved this. The miliary diffusion so very frequent in tuberculosis is of this origin. Tuberculous intestinal ulcers were found in 89 out of 161 cases of pulmonary tuberculosis coming to autopsy at Cook County Hospital.

The observations of Weigert and Benda of the histology of tubercle in relation both to the new vessels of the tubercle and to the pre-existing blood vessels is proof about as conclusive as that of Longcope and Whipple.

The next theory is that when tuberculin is injected there is a lowering of the opsonic index. This presupposes that tubercle bacilli are being discharged into the blood lymph at some time during the period of opsonic depression. There is no proof that such discharge is occurring so frequently that there is likelihood of its occurring at any given moment. So far as I know, however, there is no proof of such a spreading coincident with lowering of the opsonic index due to tuberculin.

---

* Read in the Section on Hygiene and Sanitary Science of the American Medical Association, at the Fifty-ninth Annual Session, held at Chicago, June, 1908.

It is difficult to weigh the clinical data. I have not yet read of a case in which there was a clear demonstration of cause and effect, or anything to prove or even indicate that the use of a single dose of 4 milligrams of tuberculin increased the incidence of generalizations. My autopsy experience, fairly large, has taught me that periodic partial bacillary diffusion is the rule in long continued phthisis.

In the Knopf case it is impossible to determine whether the result is coincidence or cause and effect. The Billings cases, two in number, belong in the same category. I have not been able to get the data in the Edwards and Greene cases. Letters to them elicited no more data than those given in their books and I am not able to draw a conclusion from them. Trudeau writes of a man who was to have been injected at a given time, but who had a generalization just before the proposed injection. He said: "Had the generalization followed the injection, it would have seemed an incontrovertible case."

My experience is limited to a moderate personal use extending over ten years, and a consulting relation in the hospital where it has been fairly frequently used for ten years. Results in 100 cases have been published. A second hundred cases have been studied. The Chicago Department of Health has publicly advocated its use for nearly a year, and 500 doses have been distributed. Probably in other capacities I have sent over 200 additional doses. I have heard of no ill effects in any of these cases. We are justified in concluding, therefore, that the incidence of dissemination is but low.

The certainty of the test needs no argument. The advisable dose in order to determine the limitation of discovery is a fair field for discussion.

The question now arises, do we need this means of diagnosis? This question should be asked, not of the most skilled specialists, but of the rank and file of the profession, those who are consulted before the patient has developed much of a symptomatology.

Consideration of history in the afebrile cases is of but little value in the hands of the inexperienced. Physical examination requires too much technical skill in the earlier cases for the average practitioner. Sputum examination does not reveal the disease when it is curable without great drain on the resources. Fever, rapid pulse, emaciation, sweats, are, of course, not to be considered in discussing early cases.

There is urgent need for a test easy of application, requiring no technical skill and not requiring much of experience to evaluate. With present methods for the next quarter of a century the average diagnosis will mean death after a prolonged illness.

Let us suppose, however, that there is some proof that bad results have followed the use of tuberculin for diagnostic purposes. The question next arises, is the frequency of diffusion and the degree of danger therefrom surpassed by the benefit to be derived. Diffusion is not a rare incident in consumption. It is the rule, or nearly so. Many of the resulting lesions are found cured at autopsy. The bearing of this is that diffusion, if it does result from tuberculin injection, is not as appalling as if it were otherwise unknown.

Weighing all of the factors, valuing the incidence of danger, on the one hand, and the increased curability and the decreased length of illness on the other—the possible harm, the probable gain, the weight of each—it is my judgment that no health officer with a conscience can fail to advocate the diagnostic use of tuberculin in the human subject.

A surgeon contemplating an appendectomy weighs the danger of the anesthetic and of the operation, he weighs the advantages. He acts on the balance of favor, one way or the other. Would his conscience allow him always to refuse operative procedure because there has been a rare case of death from anesthesia?

103 State Street.

ABSTRACT OF DISCUSSION

ON PAPERS OF DRS. EVANS, WHEATON AND SMITHIES

Dr. S. A. Knopf, New York: It has been said here this morning that the man who does not use tuberculin in diagnosis of tuberculosis is a man without a conscience. I am guilty of not having used tuberculin or recommended its use, except once or twice as a therapeutic means in a case when there was neither progress nor the contrary. I have the consolation of believing that in opposing tuberculin when they used to give 15 to 20 mg., I have helped in some measure to reduce the quantity to the small doses now in use. My distinguished friend, Dr. Evans, said he used 4 mg. When he said that I heard some whispering to the effect that that was altogether too much. I believe that early physical diagnosis is more carefully and frequently practiced, because of the opposition to tuberculin as a means of early diagnosis. I believe that if every practitioner would feel that the simple injection of 1 or 2 mg. of tuberculin would surely reveal the presence of tuberculosis, it would do away with physical diagnosis. I believe that careful physical diagnosis is still very important and absolutely essential as a preliminary to any one of the three tuberculin tests. That the tuberculin test is not infallible, we all know; even the tuberculin enthusiasts will admit that, but since we have so many means of using tuberculin in small and consequently less dangerous doses, I am less opposed to it. Still, even with small doses we have had the reaction in actinomycosis and in syphilis and in pure chloranemia. The examination of the sputum was once thought to be the only means of diagnosing tuberculosis, but I do not agree with that statement. It is true that you must easily find tubercle bacilli when there is a large disintegration; nevertheless, if the bacilli are not found at the first examination, then attempts should be made the second, third, fourth and fifth time; I know Dr. Brown has found the bacilli on the twentieth trial. It is something I would not wish to neglect in favor of tuberculin tests. But, of course, it must not be forgotten that while the finding of the bacilli in the sputum proves beyond a doubt the presence of a tuberculous lesion, their absence in the sputum does not by any means exclude the presence of tuberculosis.

I was very glad that Dr. Wheaton brought out the value of sunlight, for a prominent scientific man has recently made the statement that sunlight produces tuberculosis, and that the ideal way to live would be in a dark room. It will be my privilege to reply to that theory next Saturday morning before the Society for the Study and Prevention of Tuberculosis. The ideal climate to my mind is one where the patient can live outdoors the largest number of days with the greatest amount of comfort, wherever that may be. There are idiosyncrasies in the susceptibility to climatic conditions as well as to medicine. If I am called on to decide the climate for a patient, I examine my patient to see what stage he has reached and whether he has money enough to sustain him away from home for a year; and then I ask him whether he prefers and feels best in cold or warm weather. I select the climate in accordance with his preferences. The economic factor is most important. A patient who comes from the laboring classes should, as far as possible, be treated and cured in the climate where he contracted the disease. I firmly believe that the home climate of the patient, or a climate in or near the locality where he wishes to live after his restoration to health, is the ideal climate for him. It may take a little longer to cure a patient in his home climate, particularly if not ideal, but I believe that the chances of his remaining cured are better than if we had sent him to a so-called congenial climate entirely different from the one where he wishes to go back to work. If a patient is in an advanced stage, and I know he will not get well, I let him go away or stay at home, just as he likes.

Diagnosis should be begun in the schools. The Calmette or ocular test is excellent in many ways, but it is not free from danger, particularly in scrofulous children. It is necessary to be careful to avoid keratitis and other serious inflammatory troubles. Sometimes a child has been inoculated three or four times. The little ones forget that it has been done, and whether the test was made in the left eye or the right eye; and because of the sensitizing the diagnostic value is much lessened. I believe that we could accomplish a really great work in the early diagnosis of tuberculosis if we would train our school teachers to suspect tuberculosis when a child fails in its studies, looks anemic or complains of pain in the joints, and to refer such a child to the school physician for a careful examination. It is only by systematic examination and re-examination of suspected cases, that we shall find the children who are tuberculous. After a child has been declared to be tuberculous, it should be sent to an open-air school or school sanatorium. We must teach the child to love fresh air. When we begin by diagnosing tuberculosis in childhood and follow up the case so that the child will not develop full tuberculosis—you all know how curable tuberculosis is in childhood—then we shall strike at the root of the problem. Herein, I believe, lies one of the most important parts of our diagnostic work in regard to tuberculosis.

Dr. Victor C. Vaughan, Ann Arbor, Mich.: In regard to the use of tuberculin, I am midway between Dr. Evans and Dr. Knopf. Some years ago, I was using it a little and then I declared that I would never use it again. Then I used it again for a while, and then I declared I would never use it again. I am there just now. I think I shall never use it again. Of course, there are various forms of tuberculin. Dr. Smithies emphasized the point that we should know what we are using when we use tuberculin. Tuberculin is generally prepared by concentrating a glycerin culture of the bacillus of tuberculosis. In some cases the so-called tuberculin is precipitated with alcohol and re-dissolved in water and re-precipitated, etc.; in some cases it is not. More or less of the tubercle bacillus has gone into the solution. It is a powerful mixture, and we now know certainly that a proteid substance injected into the human body or administered intravenously, subcutaneously, intracranially, intra-abdominally or anywhere except in the mouth, may act as a poison. If you give two injections of egg-white at intervals, you poison the subject. By giving tuberculin you render the subject susceptible to every proteid that is in the mixture. In the hypodermic use of tuberculin I think that we should be very careful and should know what it is. I am much interested in the Calmette reaction. I do not think that the time has come when we can accept it positively. There are a few cautions yet to be borne in mind in using it. We now know, what we did not know at first, that its repeated use in the same eye may bring on rather severe inflammation. I instilled tuberculin into the eyes of 108 or 110 supposedly healthy young men in my class. Six reacted. I concluded, after a physical examination and after taking the temperature, that four of those were tuberculous. I was in doubt about one, and in one I could not find evidence of tuberculosis. That led me to believe that as a diagnostic means this reaction has its value. Twenty-one days later I made a second instillation into the same eye in each one of the students. Fifty-nine per cent. of them reacted, some violently. One young man, who was quite enthusiastic in making experiments, made a third instillation in his own eye, and the inflammation that followed was extremely violent. I did not know but that it was going to be serious. The eye was kept carefully washed out with a saturated solution of boric acid, and it healed. It is dangerous to put the tuberculin too often into the same eye. In order to have a good reaction we must learn the conditions under which we give it. I think it should be applied early. It would be a great godsend if we had an absolutely safe means of early diagnosis. I think that there is one thing about the climate that we do not always realize. I say to my patients: "You are better off in Michigan under good local conditions than in Colorado under unfavorable conditions." You can prove by statistics that the best place for consumptives is in a high latitude, in a low latitude, on the land, and on the sea. The purity of the atmosphere—local conditions—is the important point. It grows on me from year to year that pure air is the best sedative we can give consumptives to allay their coughing, and in general, I think cold, pure air is more sedative than warm air.

Dr. C. L. Minor, Asheville, N. C.: My experience has taught me to believe that the tuberculin test for the presence of tuberculosis is fully justified in skilled hands and in properly selected cases, but that its indiscriminate use by members of the profession not familiar with its administration or action can be fraught with great danger. If the profession were to use it as carelessly as a doctor of whom I have heard, who, suspecting tuberculosis in a trained nurse in his employ, without making any physical examination or taking any history, told her to come to his office next morning for a test dose of tuberculin, the harm that would be done can be easily realized. Used thus, to take the place of a proper physical diagnosis, it certainly could not be recommended. Further, it should not be used simply because of doubt. Repeated examinations and great care in every step are first necessary, but if, after such repeated examinations, you have failed to find evidence of tuberculosis, although the case is very suspicious, then the test with tuberculin is justified and proper. I believe 4 mg. to be a rather dangerously large initial diagnostic dose and that the initial dose should not be over 1 mg. It also seems to me that the distribution by the board of health to the general practitioner of tuberculin for diagnostic purposes is fraught with considerable danger. As to the relative simplicity of the different methods of giving tuberculin, the subcutaneous, the cutaneous and the ophthalmic, while the mastery of the exact doses, etc., of the former, is to the beginner a little more difficult, to any one who has once learned it, the subcutaneous method is just as easy and safe, and more accurate. However valuable a therapeutic measure may be, it must be used with intelligence. Were morphin, for instance, not used in this way, the results would be disastrous. Climate must be used with discretion. But while care will always be essential to these cases, climate, combined with care, will secure results otherwise impossible.

Dr. W. A. Evans, Chicago: My reason for advocating the dosage mentioned is that the findings which result are so definite as to be unmistakable. What we are suffering from at the present time is, I believe, a lack of definiteness of conclusion. I would not say that we should do away with physical diagnosis or valuation of history; but I take exception to the view that those are sufficient in themselves. I do not believe that there is a person here to-day who, in his life work or anything else he has set himself to do, has taken the position that the situation was being met. We all know that thousands of persons are dying because physical diagnosis and valuation of history are not sufficient to make a diagnosis when the disease can be cured. Let us hold on to everything that we have, and then search for everything that we can find. We have heard here that the indiscriminate use of tuberculin in the hands of the unskilful is fraught with danger. I trusted that we might have proof that it was fraught with danger. I have been told that this diagnostic agent should be limited to the hands of the skilful. I have yet to find any sign by which the skilful are to know that tuberculin will do harm. Until they can, I do not see why we should limit it to the hands of the skilful. I think the experiments on animals have demonstrated that it is reasonably safe. I have not yet been able to find any basis for believing that it does harm in any considerable number of cases. I do know that the valuation of history and sputum is doing harm. The consumptive at the period when there is hope for him, has to be handled by the general practitioner. I would that we could force him to go to men like Knopf who can diagnose consumption when it is curable, or Miner, but I believe that you are all of the opinion that this ideal condition will not prevail in this country. I have seen consumptives by the score going down before death cursing the members of the medical profession because they had not been told they were consumptive until they learned that there was nothing in store for them but death. We have heard that one physical examination at the hands of a man as experienced as Dr. Knopf and as Dr. Miner is not enough. We have heard that the continuous examination will eventually reveal the presence of tubercle bacilli. That is probably true. I remember that tubercle bacilli were found in a case in which they had not been found in thirteen examinations. I have been told of a case in which tubercle bacilli were found on the sixtieth attempt. You all know that when the bacillus is found on examination, the adjudication is made from one examination, and there is danger that a man will fail in his diagnosis by reason of the fact that the other fifty-nine examinations will not be made. A promiscuous use of tuberculin may here and there rarely do harm to some individual. I believe that at the same time the promiscuous use of tuberculin will mean a saving of human lives.

Dr. Vaughan has told us that the tubercle body is a multiple body, a compound, and when we inject it into our patients we poison those patients. The same holds true of morphin and chloroform. The fact is this: Everything which is powerful for good may be made powerful for harm, and the argument based on the fact that tuberculin contains poison is no better against the use of tuberculin than a parallel argument would be against the use of morphin. It does not touch the vital question, and that is: Do we add to the possibility of the discovery of the tubercle bacilli by using tuberculin? The old idea, it seems to me, has been refuted. I believe that the action on the part of the Department of Health of the City of Chicago in distributing tuberculin for the use of general practitioners will mean a saving of the lives of many of its own citizens.

Dr. Theodore B. Sachs, Chicago: The question arises if a timely and proper use of tuberculin and a correct interpretation of the resulting reaction does not require as much application and knowledge as an intelligent study of the personal history of the patient and a thorough physical examination of the chest. As an adjunct to the usual diagnostic methods, when examination and history are inconclusive, the tuberculin test has its field of application in the hands of an experienced practitioner, but always under conditions such that a proper observation of the case is possible. A point of practical importance, not to be overlooked, is the occurrence of tuberculin reaction in so-called latent cases of tuberculosis, a reaction which does not point necessarily to need of sanatorium treatment, but still is instrumental in putting the physician and patient on guard. While the practical value of ophthalmic and cutaneous tuberculin tests is still *sub judice*, the work of Birch-Hirschfeld, Calmette, Pirquet and others opens a way to modifications in the tuberculin test, divesting it of any possible harmful effects and yet preserving its reliability.

Dr. J. W. Shankland, St. Louis: I made a report on 142 cases of conjunctival and cutaneous tuberculin reaction before the St. Louis Medical Society last winter. In order to determine whether the reactions were produced by the tuberculous toxins or not, we first used the different diluting fluids and the glycerin bouillon in which no bacilli had been grown, both on the conjunctiva and the skin as controls with negative results. When tuberculin was added to these same diluting fluids, giving some positive results, it was proof enough that the tuberculin was the cause of the reaction. By physical examinations and microscopic work the cases were classified as follows: 1, positively tuberculous; 2, suspected tuberculous; 3, non-tuberculous with other diseases, and 4, clinically normal individuals. The general average of the cutaneous reactions in these four classes of cases shows about 50 per cent. positive. In this series of cases the conjunctival reaction fell to 25 per cent. positive. The cases in Class 3, of other diseases, gave a general average of 37 per cent. positive reactions in the 700 patients inoculated. The results of the various men working with tuberculin vary so greatly, both in the work with animals and in that with people, that at times their reports are precisely opposite; thus destroying confidence in both the conjunctival and the cutaneous reactions. I think that a great deal of work must yet be done with tuberculin before we can come to a definite conclusion as to its real diagnostic value. It would therefore be infamous to advise an individual giving a positive result to either of these reactions to leave his business and his family to seek a different climate. It is impossible to make the diagnosis without the corroboration of other findings. If tuberculin is a specific, then such advice would be possible without the consideration of other facts. As it now stands, tuberculin may be an aid to diagnosis in adults, and yet there is a great deal to be proved as to just what value as an aid these reactions are in the adult cases. Dr. Engelbach, my associate in this work, has inoculated a large number of perfectly healthy individuals in the St. Louis University; among them, a number of football players and athletes in the pink of condition. He reports positive cutaneous reactions in 50 per cent. and positive conjunctival reaction in 25 per cent. of this series of cases. We have simultaneously inoculated patients on the skin and in the eye, and would get a positive conjunctival reaction in a given case, with a negative cutaneous reaction, while in another case the result would be the reverse. We must account for this variance, and how are we going to do this in a perfectly healthy individual? To prove the relations of these reactions to the pathologic conditions found seems to me as impossible as it is to send a telegram from one city to another with the wires severed midway between the starting point and the finish. We put a drop of tuberculin in the eye, and we see the reaction follow; there the message stops. What is back of that reaction in the way of a lesion we are unable to say because we get positive reactions when no pathologic findings are present, and the degree and the kind of reaction bear no definite relation to the location, extent or activity of the lesion when one is found at autopsy. Every symptomatic message should be traceable to a functional or pathologic base.

Dr. H. M. Kinghorn, Saranac Lake: It is our custom at Saranac Lake to begin with a small dose of tuberculin. Of course, we do not give the tuberculin test to any patient until we have used all other tests in making the diagnosis. When we have made a careful examination of the chest and of the sputum, if we think that there is tuberculosis present, we then give the tuberculin test. First of all, we take the temperature every two hours for two or four days. We give the test only if there is no elevation over 99.2. We then give the first test of 0.5 mg. in the evening. We regard a reaction of one whole degree above the highest point of the temperature on the previous days as definite and an elevation of less than a degree as suspicious. We then wait until the temperature has become normal and we either repeat that dose or give a larger dose. I feel that it is wiser to increase the dose from 0.5 to 2 mg., so that within two days or three days we give a second dose of 2 mg. If we get a definite reaction, of course that makes the diagnosis. If we don't get a definite reaction from 2 mg. we increase to 5 mg. after an interval of two or three days, and then to 8 and 10 mg. at intervals of two or three days. It is a very valuable thing in some cases in which the disease is strongly suspected to repeat the dose of 10 mg. I am quite sure that some cases are missed if one does not go to 10 mg. I have used the test for ten years and I have never had any bad results. Of course, the cases in which it was used were incipient cases or they would not have had the test. They were without fever. The only danger I can see in the test is from the reaction. In addition to using tuberculin for test purposes I have used it for treatment, treating as many as twenty patients in private practice at one time. All these patients will some time or another have a reaction, and I have no fear from the tuberculin reaction. Sometimes the reaction may be prolonged for several days or even a week, but I would console the beginners who are using tuberculin by saying that the temperature will become normal if they will only keep their patient quiet and absolutely at rest. I feel as strongly as Dr. Evans and Dr. Miner do about the great value of the test. I think it is one of the finest things we have in medicine. Of course, it is to be used with great care, and the dose should be put up by some one who has had experience in the metric system when the general practitioner intends to give tuberculin injections. There will then be no mistake in the dosage.

Dr. C. C. Browning, Los Angeles, Calif.: I endorse what Dr. Evans and Dr. Kinghorn have stated. I think dosage depends somewhat on how we are going to control our patients. In a sanitarium, where I expect to have the patient under my control, I much prefer the small dose. In addition to watching over the temperature I watch over the physical signs. Of course, I use the tuberculin test only when it is necessary to clear up an obscure case. If there have been suspicious symptoms they will be frequently augmented. It is possible that the temperature rise may be brought about by nervousness. At the time I am taking the temperature I am constantly watching until I become quite familiar with those signs. If my patient happens to be one from whom I am not likely to hear again, and it depends on what we do at one time for him, then I think that probably the larger dose is better. I have no fear of the ordinary tuberculin reaction. I have used tuberculin for years, and for the past few years have had from 75 to 100 patients under my care continuously, and any ordinary reaction I think is absolutely without danger. I think one of the great opportunities for preventive medicine is to begin teaching in the schools. We should give the pupils good ventilation. If a tuberculous patient is to be treated in a home success will be attained by making home conditions approach those of a sanitarium. I do not feel that, because it is possible that a person's temperature may be raised by the direct rays of the sun, therefore a climate in which there is a great amount of sunshine may necessarily be detrimental to that person. I do not think that there is any "best" climate for all patients. Each patient should be studied carefully, thoroughly and scientifically before a climate is recommended, just as before the administration of any medicine.

Dr. Gordon Wilson, Baltimore: I do not think that enough stress has been laid on the dangers of the ophthalmic reaction. The European papers have mentioned a considerable number of cases of ulcer of the cornea and recurrent conjunctivitis following its use. My experience in its use has been only in the case of persons suspected of having the disease. I have had nearly one hundred cases, and so far the reactions have not been very severe. The most severe results that I have had have been edema about the eyes, and conjunctivitis, lasting about a week. In Baltimore there has been one bad case of ulcer of the cornea in a child who had bone tuberculosis, to whom a single dose was given according to Calmette. It was in a hospital for tuberculous children, where the chances for secondary infection were slight, and as soon as the reaction took place the usual treatment for conjunctivitis was instituted. I heard night before last of a doctor in Denver, Colo., who tried it on himself, and he had a severe conjunctivitis. Since then he has noticed that after reading late at night the conjunctiva of that eye is markedly injected on the following morning. I think that we are dealing with a dangerous agent, dangerous because used on a very important organ of the body. The danger of secondary infection is present in both the ophthalmic and the skin test, but there is less danger from secondary infection when injected in the skin.

Dr. C. H. Johnston, Grand Rapids, Mich.: What constitutes a reaction? Dr. Kinghorn says that a reaction in his mind simply consists of an elevation of temperature of one degree. This is not the belief of all of Dr. Kinghorn's colleagues. Two of them have told me repeatedly that, in addition to the elevation of temperature, there must be some other indication, such as backache, or headache, or muscular pains. In Dr. Kinghorn's opinion, is a simple rise of temperature alone, without any other indications, enough for us to base a diagnosis of a reaction on? I hope to-day to get some definite information on the relative importance or reliability of the ocular as compared with the hypodermic test, because in the last few months, in ten different cases, I got no reaction with the eye test, but got a reaction with the hypodermic test. One of my friends said to me that it was probably due to the material that the test was made with, but the material in these cases was the same as was followed by positive reaction in other cases.

Dr. H. M. Kinghorn, Saranac Lake: The temperature is the important point in a reaction. When you have a temperature of one degree over the highest previous temperature, and that one degree of temperature has been rising slowly, any one who has had any experience with the tuberculin reaction will understand that this is characteristic. The temperature rises slowly, and then drops. Even without other symptoms I regard it as very definite. You only occasionally meet patients who will have a temperature of 101 without any other constitutional symptoms except a rapid pulse. That occasionally occurs. Usually, however, with that rise in temperature you will have a definite feeling of malaise, which accompanies the tuberculin reaction, also headache, loss of appetite, pains and aches all over, and very frequently a large lump at the seat of the injection. All this constitutes a tuberculous reaction. However, where the temperature rises slowly I regard it as a definite reaction without those symptoms.

Dr. S. H. Gilliland, Marietta, Pa.: I have prepared much of the tuberculin for use. It has been said that tubercle bacilli may be found in suspension. If the tuberculin is prepared according to the original method of Koch it is impossible to have tubercle bacilli in suspension. As Dr. Vaughan said, after they have grown on the glycerin beef broth the tubercle bacilli are then removed from the beef broth by triple filtration. You must see that the filter is efficient and that the organisms do not go through. The filters I use are tested in this way: A virulent culture of tubercle bacilli suspended in salt solution or media is filtered and the filtrate injected into guinea-pigs, thus determining the efficiency of my filters. I can then feel positive that the filtrate is free from tubercle bacilli. Dr. Smithies brought out the point that for human beings afflicted with tuberculosis the tuberculin should be made from the tubercle bacilli of human type. I am at a loss to understand that statement, as I have made tuberculin from tubercle bacilli of bovine type, and have obtained equally reliable results. It is an accepted fact that a number of cases of tuberculosis are of direct bovine origin. I have supplied material for about 12,000 tests. That excludes the subcutaneous test, but of the other tests the majority were ophthalmic. I have heard of no bad or unsatisfactory results. I have heard of all the work that has been done in this country through the use of my tuberculin, bad and good, and in a series of cases in which a man made three tests in one person the results were almost absolutely uniform. That has not been the case in certain other countries. The eye test has given a positive reaction and the cutaneous test has failed, and vice versa. In these cases the tuberculin was all prepared from the same strain of tubercle bacilli. I believe that the eye test is one with which a certain degree of danger is associated, and I do not believe that the physician is fully justified in using it freely to diagnose any condition in the body; that is, provided we have another test, and I feel that we have other tests that are equally reliable, at any rate in children. Whether they are so in adults remains to be seen.

Dr. M. P. Ravenel, Madison, Wisconsin: I agree with what Dr. Kinghorn has said most thoroughly and believe that tuberculin should be used in every doubtful case. I am sorry that Dr. Knopf has apparently approved the diagnosis by bacilli in the sputum. I think that is one of the worst doctrines that has ever been taught in regard to diagnosis, and am thoroughly convinced that it is responsible for the death of many people. Bacilli can appear in the sputum only after softening and breaking down of the tubercle has taken place. In the great majority of cases this means secondary infection, and a diagnosis based on such findings can not be considered an early one. I believe that the tuberculin test in doubtful cases will enable us to make a much earlier diagnosis than this, and in this way many lives will be saved. I can not entirely agree with Dr. Evans as to the wisdom of putting it in the hands of general practitioners, although I have no doubt that every educated physician can learn its proper use. At the present time it is best used by specialists. I can not agree that this is saying anything against the practitioner, any more than it is to say that the general practitioner should not attempt an oöphorectomy. I am sure that the general physician does not regard it as an attack on him when one advises that cases of surgery go to a surgeon, and at the present time it is the same thing with regard to the tuberculin test. In regard to what constitutes a reaction, if temperature alone is taken as an index, mistakes may be made. It is, of course, a part of the symptom-complex, and a most important part, but should be taken in connection with all other symptoms, subjective and objective. The diagnosis should not be made on any one particular symptom. The point made by Dr. Sachs is well taken. I have recently, in some experiments with tuberculin in the shape of ointment, observed a typical reaction in two men who were in the best of health, one of whom more than a year ago had a cutaneous tubercle. Neither of these men was a subject for sanitarium treatment. While these are special cases, there are many others who will give the tuberculin reaction but who are not fit subjects for sanitarium treatment.

Theoretically, the proposition was correctly stated by Dr. Knopf, that the climate which enables the patient to spend the greatest amount of time in the open air with least expense of vital force is the best one for the treatment of tuberculosis. Practically, this does not seem to hold true. I do not know of any place in any country where better results are obtained than at Saranac Lake, and yet it can not be called an ideal climate according to the standards laid down. I believe that there are certain patients who do better in a selected climate, but that most patients should be treated as near their homes as possible. Sending people hundreds of miles away from home without friends and without money is one of the most cruel things that can be done. More important than climate is the personality of the attending physician. The man who has his patients under strict discipline and who is able to inspire them with hope and courage is the man who gets the best results regardless of what the climate is.

Dr. Charles L. Minor, Asheville, N. C.: I admit that climate without care is almost useless, since the results obtained will be only temporary; but I also maintain that except in unusually favorable cases the best results are not likely to be obtained with care but without climate, and any one, by the use of a little thought, must realize, unless he is so prejudiced as to have his mind closed to conviction, that the combination of these two good things will give the best results.

Dr. S. A. Knopf, New York: About ten years ago, in my first book, I stated that to find the bacilli was absolute proof of the presence of tuberculosis and that not finding them did not exclude the possibility of a pulmonary tuberculosis. I stated distinctly this morning that, as a rule, we find the bacilli only when disintegration has taken place, but this should not be an excuse for not looking for them. I also have been misunderstood in regard to my attitude as to tuberculin. We have now some tuberculin test methods which are relatively free from danger, such as the skin method, the use of which may be justified in rare instances. After the patient's history has been taken and a careful physical diagnosis has been made, he should be informed of the consequences of the tuberculin test. His permission, and that of his family physician, and the approval of the practitioner's own conscience, should be obtained before making the test. How many of you would be willing to have 4 mg. of tuberculin injected into you without a previous physical examination justifying it as a last resort? I still plead with you not to neglect what our fathers have taught us, a careful taking down of the history, and a still more careful physical diagnosis.

Dr. Frank Smithies, Ann Arbor, Mich.: In the routine work of teaching physical diagnosis I have had ample opportunity of observing the effects of both the subcutaneous and the conjunctival reactions to tuberculin. I agree heartily with Dr. Knopf that no form of tuberculin test can take the place of accurate physical examination with the patient stripped. But there are many patients about whom, even after careful examination, one is in doubt. In these some variety of tuberculin test is indicated. I have faith in the ability of the general practitioner to make a reliable test with tuberculin subcutaneously administered, if the practitioner will only take the time to do so. In general practice the conditions are entirely different from those in hospitals or sanatoria, and as a consequence the details connected with the proper administration of tuberculin subcutaneously are more difficult to see to, and as a result the method does not always yield dependable information. I had these facts in mind when I took up the study of the conjunctival reaction, and my endeavor was to secure figures for a dependable and at the same time a conveniently carried out test. I am still inclined to the belief that where men have presented figures from sufficiently large series of cases the results have been favorable to the use of the conjunctival test. Of course, it is quite useless to compare the majority of the German reports with those from the French, inasmuch as in Germany there seems to be a prejudice against the test, largely on account of Calmette's name being associated with it. Then again, the tests have been made in Germany with a great variety of tuberculin preparations, many of which are now recognized as being unfitted for the work. I admit that here and there serious consequences have followed the conjunctival test. I called attention to four violent reactions in the work of Dr. Walker and myself this morning. I know of no case, however, in which such results have followed when the eyes were negative before the test was administered and were looked after following the instillation of the tuberculin. Regarding the different varieties of preparation used, I believe that when possible we should use tuberculin from human bacillus growths when testing human beings. In my opinion, the work of Detre with the cutaneous reaction seems to prove that more distinct manifestations are secured in tuberculous subjects when tuberculin from human bacillus growths are used, in preference to bovine bacillus growth tuberculin. I believe that many of the commercial tuberculin "discs" are not dependable.

THE DIAGNOSTIC VALUE OF THE CUTANEOUS AND CONJUNCTIVAL TUBERCULIN REACTIONS *

WILLIAM ENGELBACH, M.D.

AND

J. W. SHANKLAND, M.D.

ST. LOUIS

In endeavoring to arrive at definite conclusions as to the diagnostic value of the recent local tuberculin reactions, we have made a study of the literature on this subject to May 1, 1908, to which we have added the results of personal observations on 1,242 cases. The review of the literature includes the opinions of nine authors on their results with animal experiments; the reports of 41 authors on 5,032 cases of all ages subjected to these reactions, 3,477 to the conjunctival reaction and 1,546 to the cutaneous reaction. Our own investigations were made on adults only at the St. Louis City Hospital and the St. Louis University Medical School. They consist of 499 cutaneous reactions and 743 conjunctival reactions on 125 positive tuberculous cases, 190 suspect tuberculous cases, 700 other diseases not tuberculous clinically and 90 clinically normal individuals. The sum total of all cases considered is 6,305.

---

* Read in the Section on Practice of Medicine of the American Medical Association, at the Fifty-ninth Annual Session, held at Chicago, June, 1908.

* Owing to lack of space, the article is here abbreviated by the omission of the portions relating to technic and histology as well as some of the case reports and tables. The complete article appears in the Transactions of the Section and in the authors' reprints.